IN THIS ISSUE

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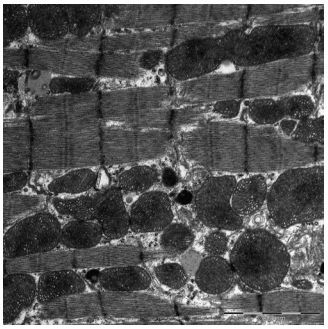
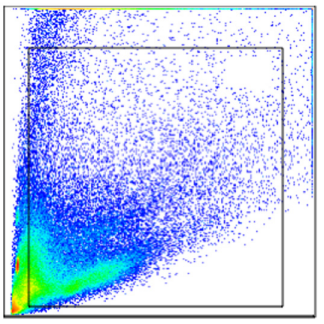


Quaking Inhibits Doxorubicin Cardiotoxicity (p 246)

An RNA-binding protein called Quaking protects heart cells from toxic chemotherapy, report *Gupta* et al.

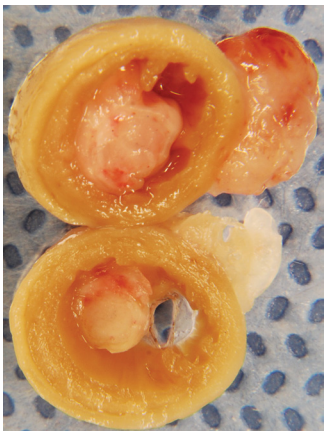
The cancer drug doxorubicin is cardiotoxic; it causes myocardial apoptosis and atrophy that can ultimately lead to heart failure. Developing less toxic chemotherapeutics would be ideal, but in the interim, there is immediate clinical need to reduce the cardiotoxicity of doxorubicin, without impairing its efficacy. For this, it is important to develop a thorough understanding of the molecular pathology of doxorubicin-induced cardiotoxicity. Gupta and colleagues performed transcriptome analysis on the hearts of mice treated or not treated with doxorubicin. Among the many RNAs differentially expressed, they found significant down-regulation of Quaking (Qki) in treated hearts. This circular RNA-regulating protein has been previously shown to prevent apoptosis during myocardial injury. Indeed, the team found that not only were some circular RNAs misregulated in the doxorubicin-treated hearts, but that over-expression of Qki attenuated doxorubicin-induced cardiac myocyte apoptosis and atrophy in vitro and in mice. These results suggest that boosting levels of Qki in patients receiving doxorubicin chemotherapy may be a potential means of protecting their hearts from the drug's toxic effects.



MSC Immunomodulation and Atherosclerosis (p 255)

Mitochondrial oxidative stress reduces MSC immunopotency in atherosclerosis sufferers, report *Mancini* et al.

Mesenchymal stem cells (MSCs) are known for their natural immunomodulatory properties and, as such, have been used in clinical trials to treat coronary artery disease caused by atherosclerosis. But results from these trials have been less promising than expected: in part because autologous MSCs from atherosclerosis patients have impaired anti-inflammatory capacities. Mancini and colleagues investigated the molecular underpinnings of this reduced potency, and they found evidence showing that mitochondrial oxidative stress is increased in patient cells. They analyzed MSCs from 80 individuals with and without atherosclerosis and discovered that cells from patients with atherosclerosis had increased levels of reactive oxygen species (ROS), and were less effective at suppressing T-cell proliferation in vitro than those from healthy individuals. Furthermore, pharmacological reduction of ROS levels in the MSCs from atherosclerosis patients lowered inflammatory cytokine production and improved the T-cell–suppressing effects. Together, the results indicate that lowering mitochondrial oxidative stress in autologous MSCs may improve the efficacy of these cells for treating coronary artery disease.



iPSC-EVs for Myocardial Repair (p 296)

Extracellular vesicles offer safe and effective alternative to iPSC therapy for myocardial infarction, say *Adamiak* et al.

The therapeutic use of stem and progenitor cells for treating injured myocardium has been extensively investigated in both animals and patients, but the results so far have shown only modest efficacy. It is currently believed that these cells act as a source of secreted factors to promote regeneration and that such paracrine effects could be delivered either directly or via extracellular vesicles (EVs)—small membrane-bound packages of cellular contents. Adamiak and colleagues, therefore, investigated whether EVs exert beneficial factors and if so, whether these vesicles alone could provide effective treatment. They examined the contents of EVs from mouse induced pluripotent stem cells (iPSCs) and found that they contain an abundance of proangiogenic and cytoprotective factors. In agreement with these findings, they found that when the EVs were transplanted into the hearts of mice after myocardial infarction, the vesicles promoted healing and heart function more effectively that iPSCs themselves. Importantly, although many of the mice injected with iPSCs developed cardiac tumors, no tumors were observed in the EV-treated animals. The authors conclude that EVs may be a safer and more effective option than iPSCs for treating infarcted hearts.

Written by Ruth Williams

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